

WHAT IS CLAIMED IS

1. A modified pokeweed antiviral protein (PAP) having one or more modifications relative to wild-type PAP within one or more regions other than the active site such that the activity of the modified PAP towards viral RNA is increased relative to wild-type PAP.
2. The modified PAP of claim 1, wherein the viral RNA towards which the modified PAP has increased activity is retroviral RNA.
3. The modified PAP of claim 2, wherein the retroviral RNA is HIV-1 RNA.
4. The modified PAP of claim 2, wherein the HIV-1 RNA is RNA of drug resistant HIV-1 strain.
5. The modified PAP of claim 1, wherein the activity of the modified PAP is decreased towards ribosomal RNA relative to wild-type PAP.
6. The modified PAP of claim 1, wherein one or more of the modifications alters the relative conformation of one or more amino acids which is at least partially buried in wild-type PAP.
7. The modified PAP of claim 6, wherein one or more of the modifications is within a hydrophobic region of PAP.
8. The modified PAP of claim 7, wherein one or more of the modifications is within α helix 4-loop- α helix 5 region.
9. The modified PAP of claim 8, wherein one or more modification comprises a modification at one or more of the following amino acids: 76, 151, 152, 158, 162, or 166.
10. The PAP of claim 9, wherein amino acid 151 is modified.

11. The modified PAP of claim 10, wherein the modification at amino acid 151 is a mutation from lysine to alanine.
12. The modified PAP of claim 9, wherein amino acid 152 is modified.
13. The modified PAP of claim 10, wherein the modification at amino acid 152 is a mutation from isoleucine to alanine.
14. The modified PAP of claim 7, wherein one or more the modifications is within the C-terminal portion of α helix 6.
15. The modified PAP of claim 14, wherein one or more modification comprises a modification at one or more of the following amino acids: 13, 16, 142, 188, 191, or 192.
16. The modified PAP of claim 15, wherein the modification is at amino acid 191.
17. The modified PAP of claim 16, wherein the modification at amino acid 191 is a mutation from phenylalanine to alanine.
18. The modified PAP of claim 15, wherein the modification is at amino acid 192.
19. The modified PAP of claim 18, wherein the modification at amino acid 192 is a mutation from asparagine to glycine.
20. The modified PAP of claim 1, wherein one or modification is one or more amino acid substitution, wherein the substitution comprises:
K151A, I152A, F191A, N192G, or combinations thereof.

21. The modified PAP of claim 20, wherein the substitution comprises K151A and I152A.
22. The modified PAP of claim 20, wherein the substitution comprises F191A and N192G.
23. A composition comprising a modified PAP according to any of claims 1-22 and a pharmaceutically acceptable carrier.
24. The composition of claim 23 further comprising one or more antiviral compound, wherein the antiviral compound is a nucleoside analog reverse transcriptase inhibitor (NRTI), non-nucleoside analog reverse transcriptase inhibitor (NNRTI), protease inhibitor (PI), or combinations thereof.
25. A method for inhibiting viral replication comprising contacting the virus with a modified PAP according to any of claims 1-22.
26. The method of claim 25, wherein the virus is human immunodeficiency virus (HIV).
27. The method of claim 26, wherein the HIV virus is HIV-1 virus.
28. The method of claim 27, wherein the HIV-1 is a drug resistant HIV-1 virus.
29. The method of claim 28, wherein the wherein the drug resistant HIV-1 virus is a resistant to one or more of the following drugs: nucleoside analog, non-nucleoside analog, or protease inhibitor.
30. A method for inducing depurination of viral RNA comprising contacting the virus with a modified PAP according to any of claims 1-22.

31. A method for treating viral infection in a subject in need thereof, comprising administering to the subject an effective anti-viral amount of a modified PAP according to any of claims 1-22.
32. Use of a modified PAP according to any of claims 1-22 to inhibit viral replication.
33. Use of a modified PAP according to any of claims 1-22 to induce depurination of viral RNA.
34. Use of a modified PAP according to any of claims 1-22 in the manufacture of a medicament for treatment of a viral infection.